

004T60" 226T960

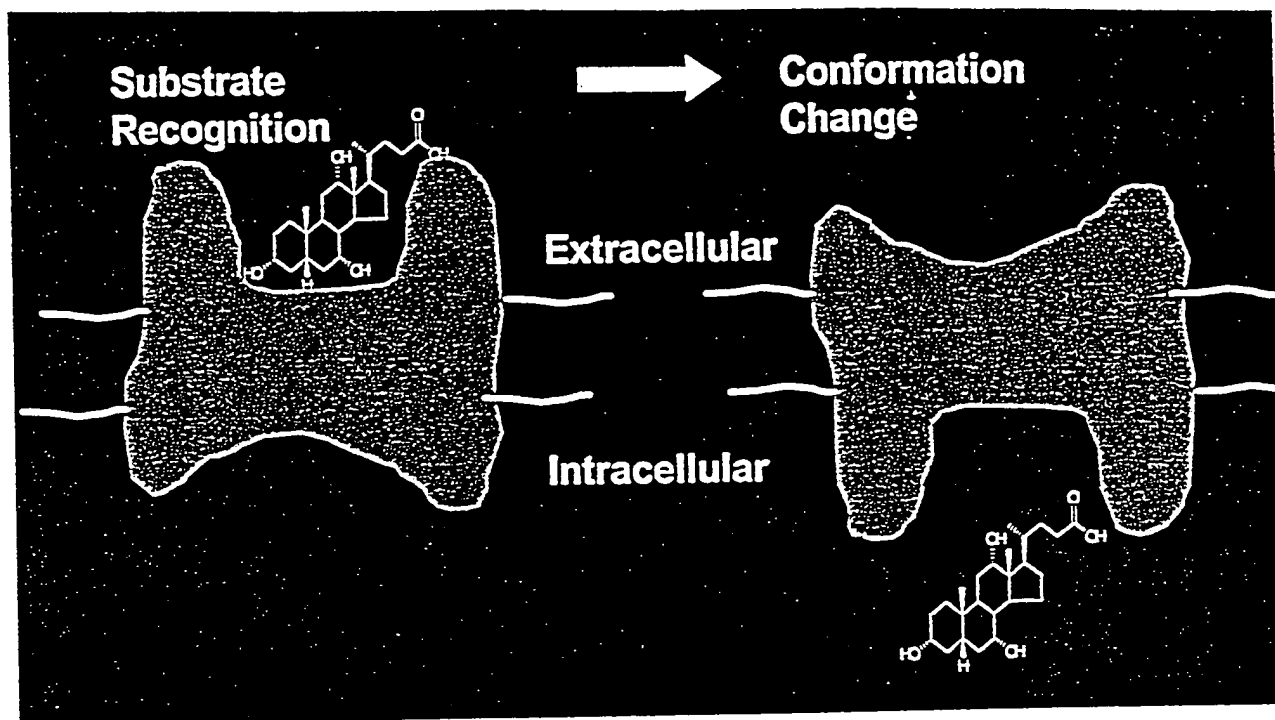


FIG. 1

DDHFSO" 226T9960

Intestinal lumen

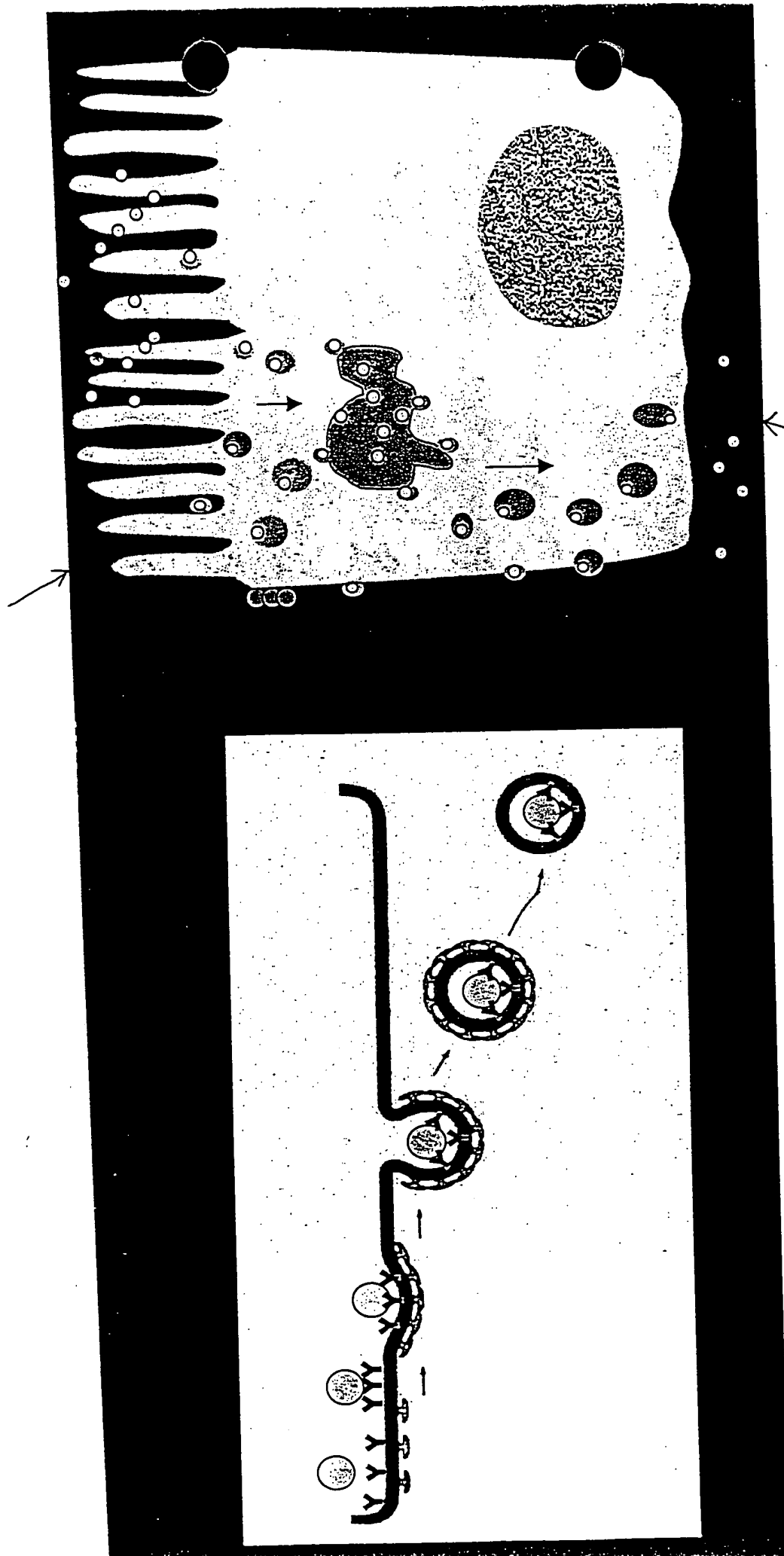


FIG. 2B

Blood

FIG. 2A

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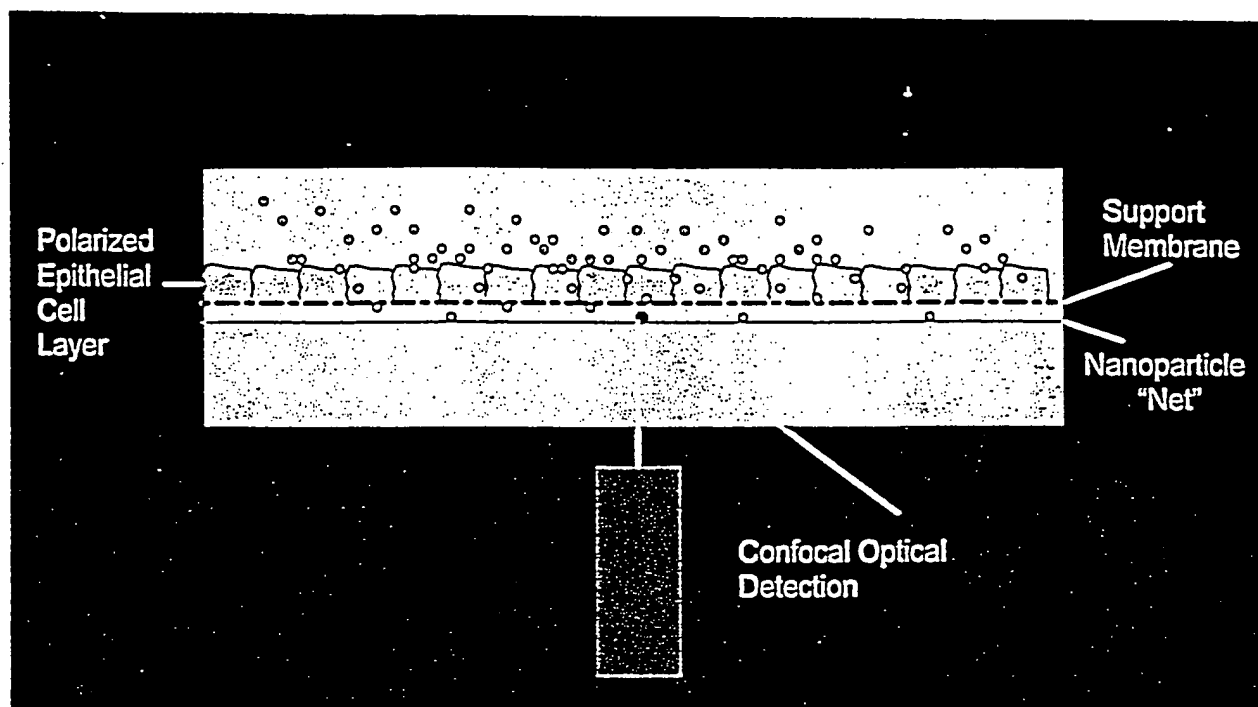


FIG. 3

Substrate-mediated Efflux "Trans-stimulation"

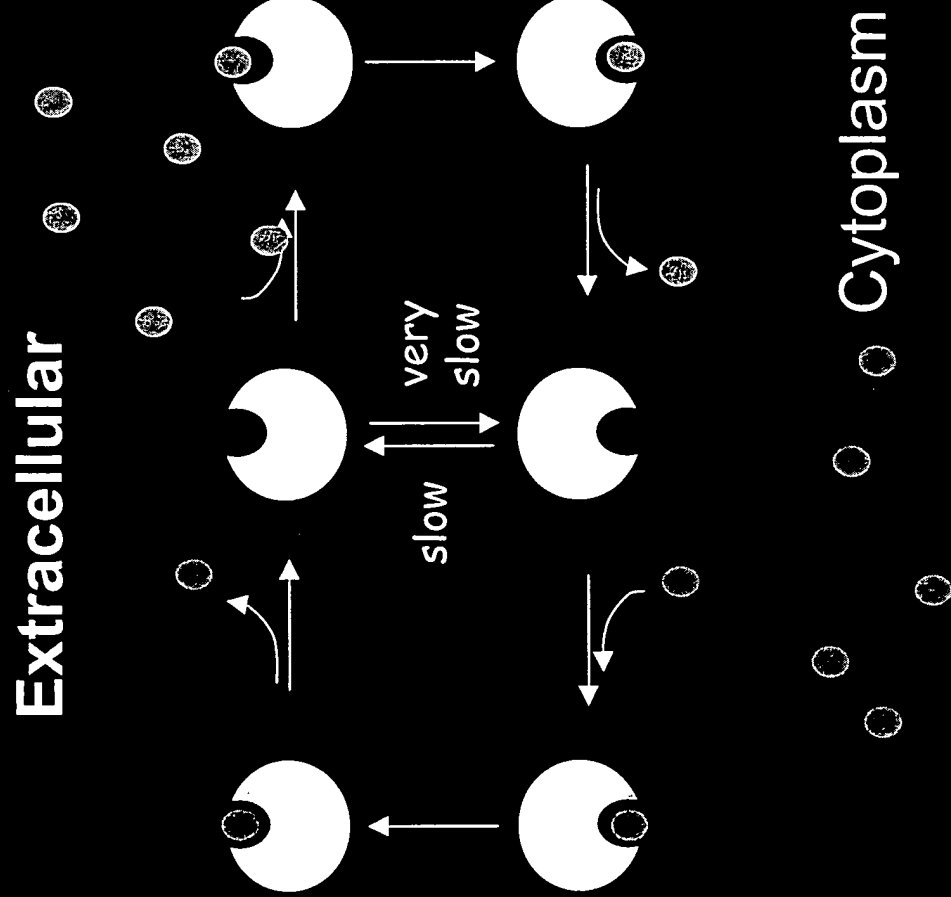


Fig. 4

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Uptake of XP10486 into CHO and CHO-PEPT1 cells

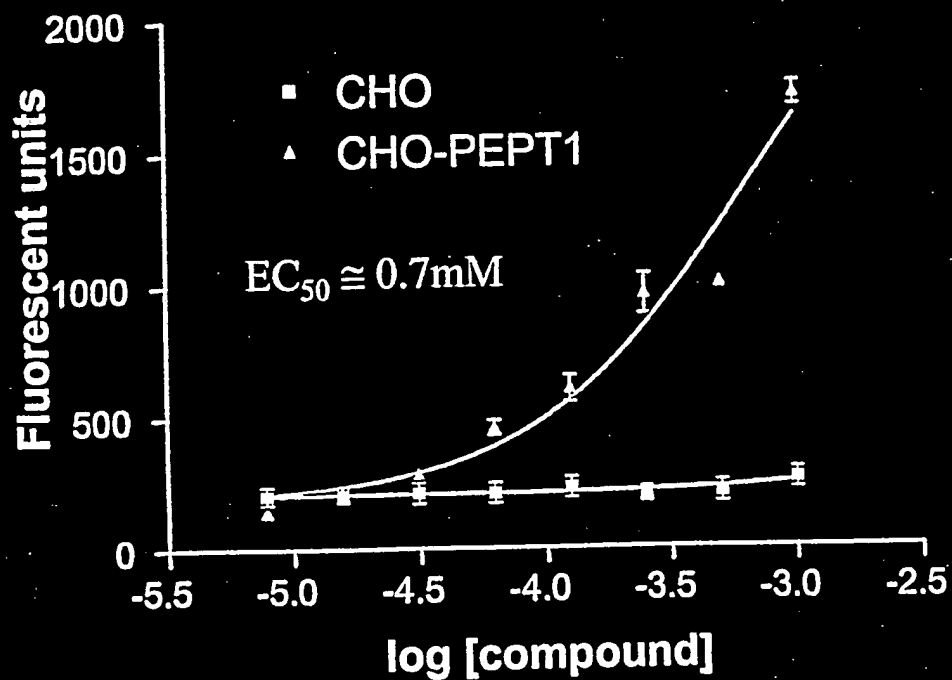


FIG. 5

LBAT Competition in 96 and 384 Well Formats

Fig. 6A

96 Well

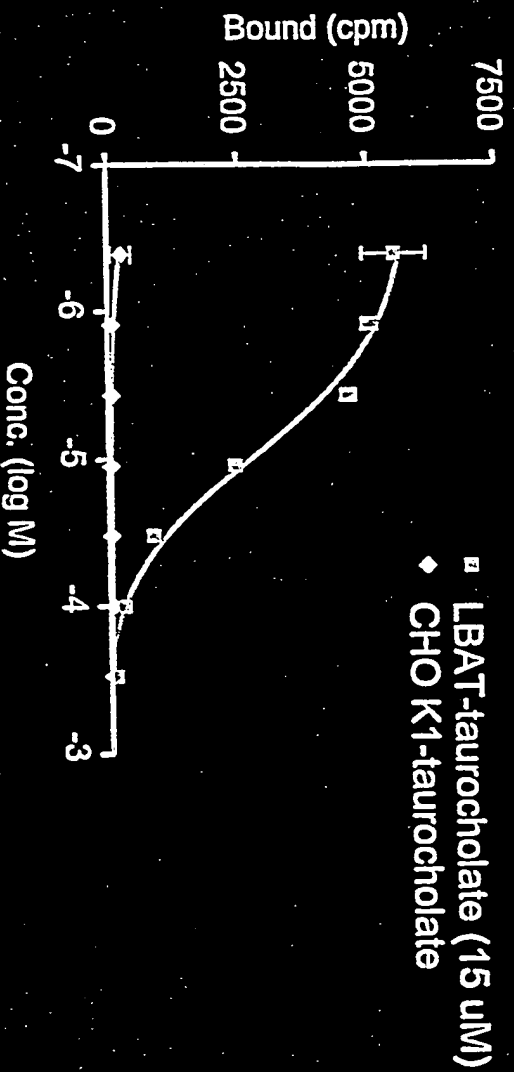
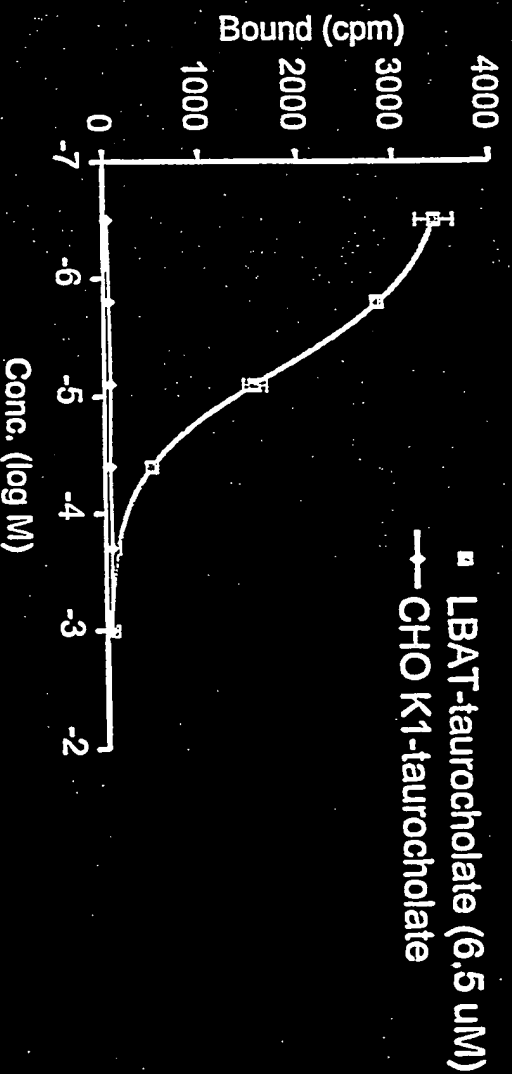


Fig. 6B

384 Well



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10 Pools from 200-Member Fluorescent Dipeptide Library

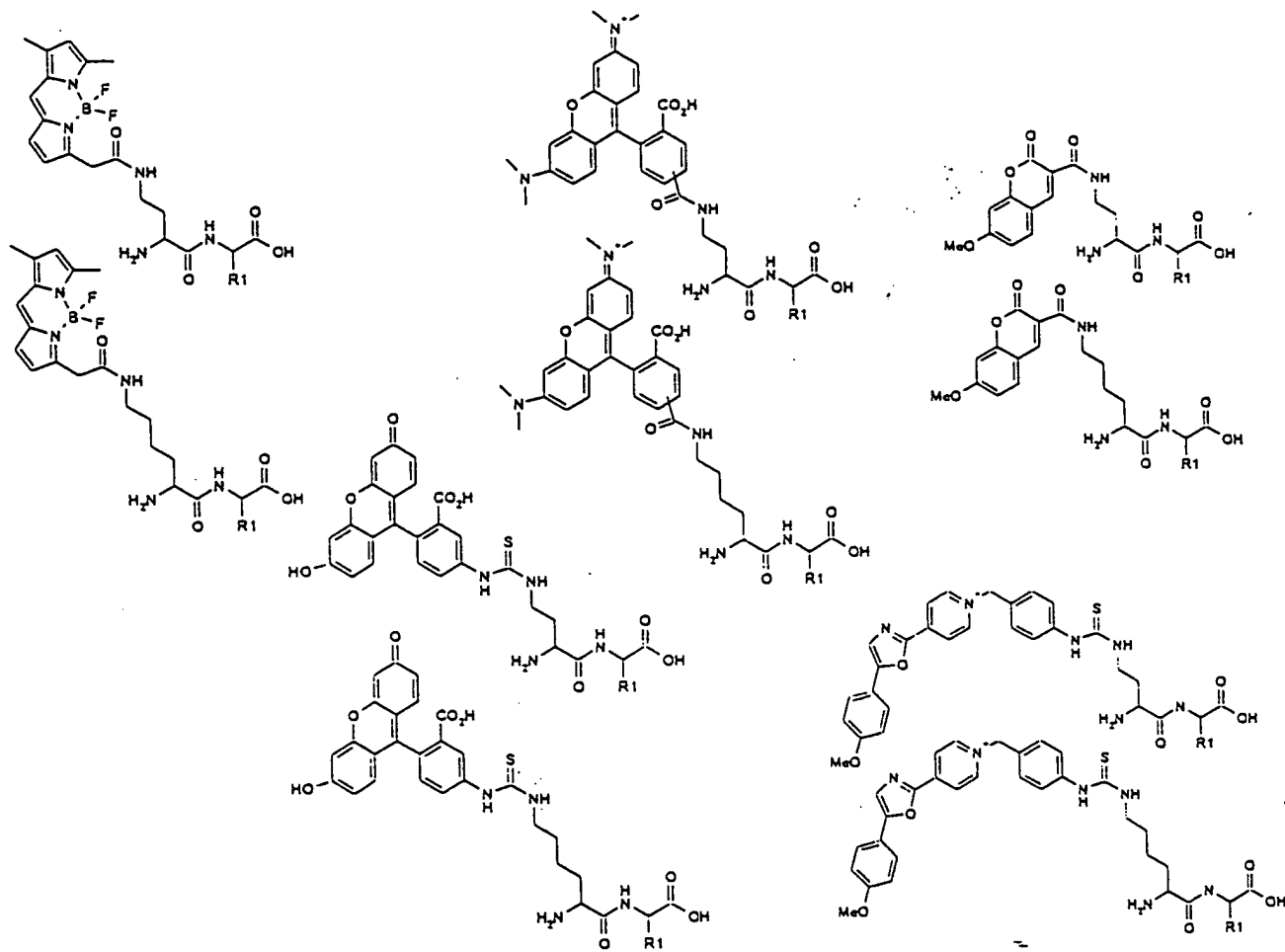


FIG. 7

Synthesis of a Dipeptide Library

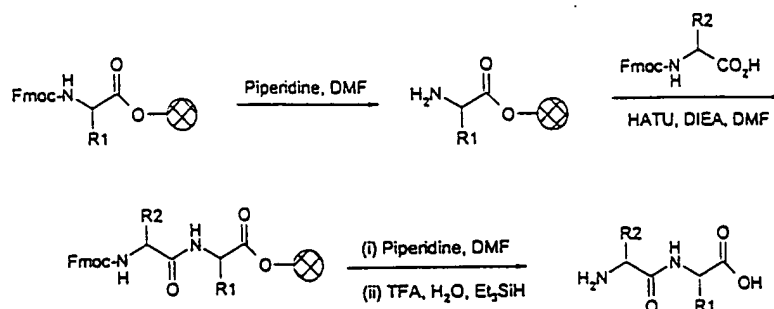


FIG. 8

Synthesis of β -Lactam Library

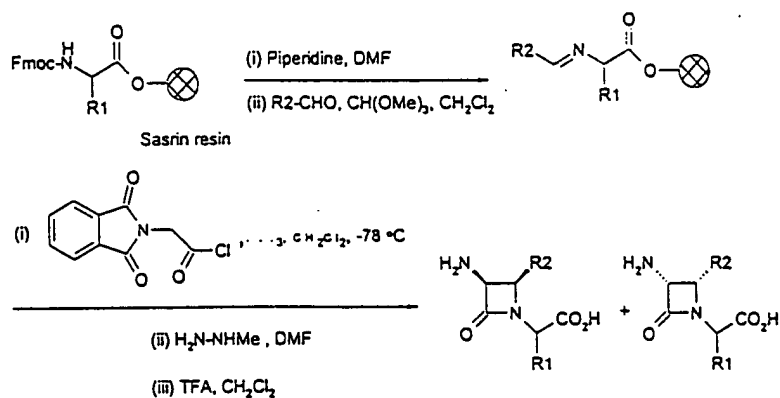


FIG. 9

Synthesis of Fluorescent PEPT1 Substrate XP10486

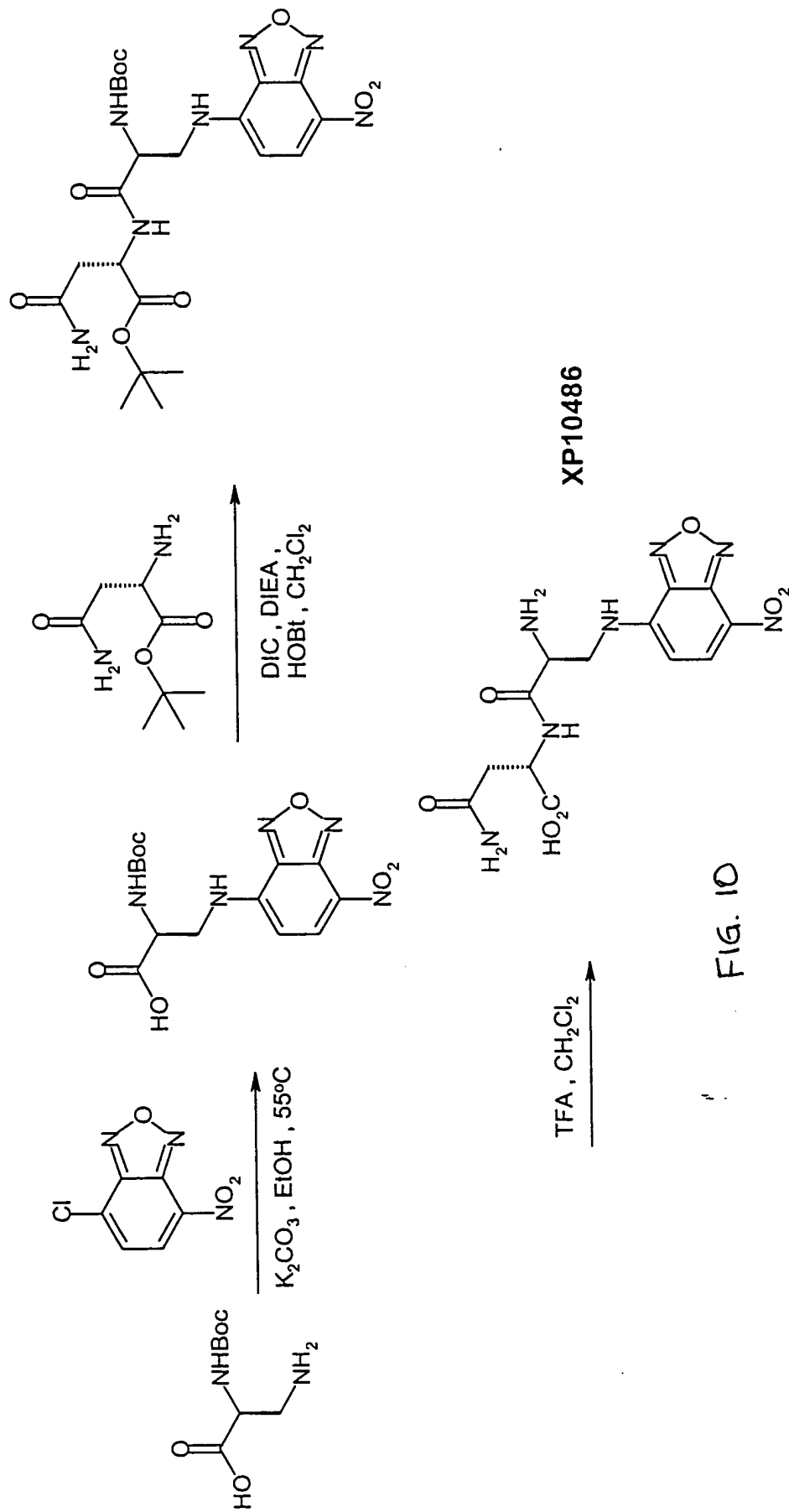


FIG. 10

Using Combinatorial Potential of Dipeptide Motif to Rapidly Establish

Structure-Activity Relationships for PEPT1

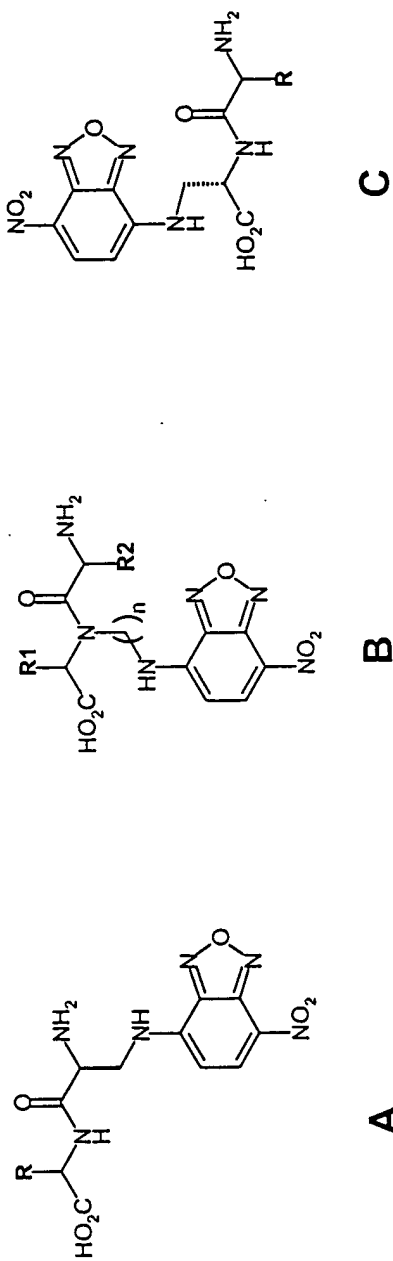


FIG. 11

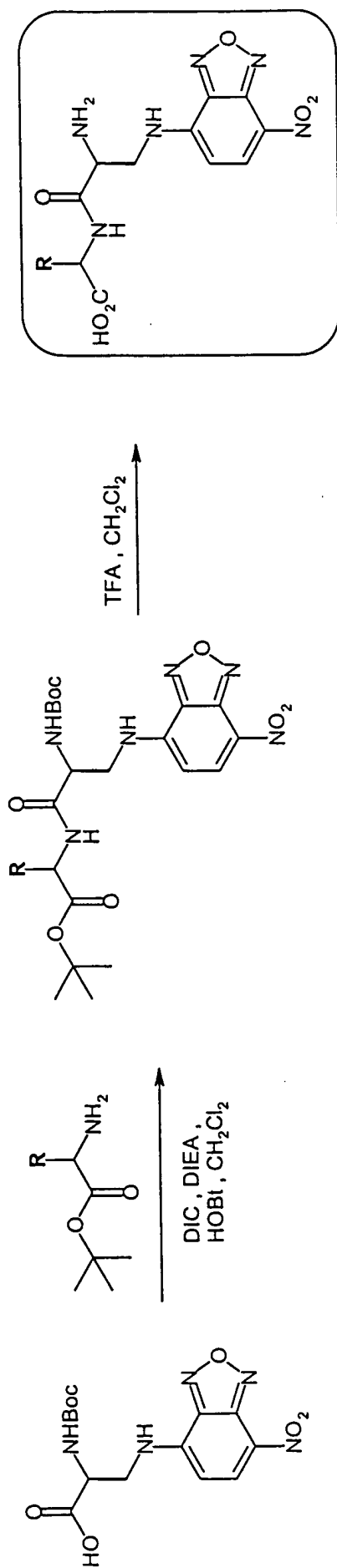
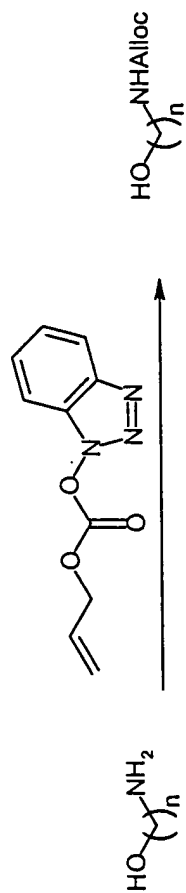
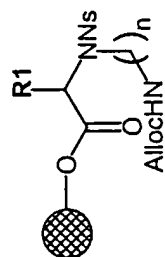
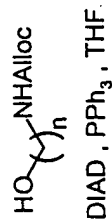
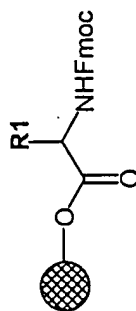
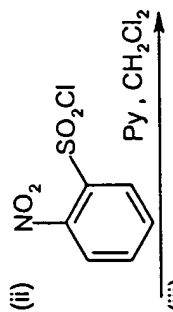


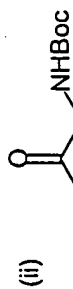
FIG. 12



(i) Piperidine, DMF



(i) PhSNa, DMF



DIC, DIEA, HOBT, CH₂Cl₂

(iii) [Pd(PPh₃)₄], Me₃SiN₃, THF

(iv) NBD-Cl, K₂CO₃, EtOH

(v) TFA, CH₂Cl₂

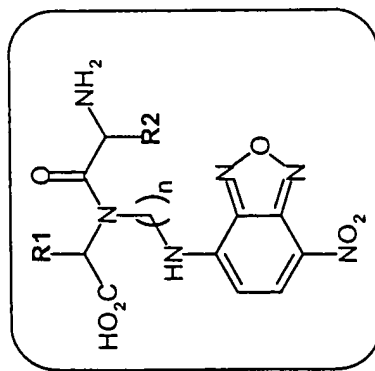
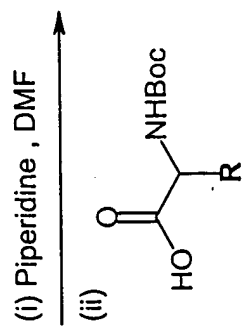
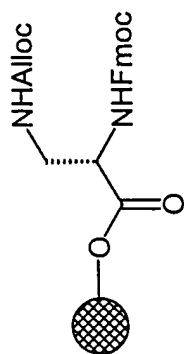


FIG. 13



DIC, DIEA, CH₂Cl₂

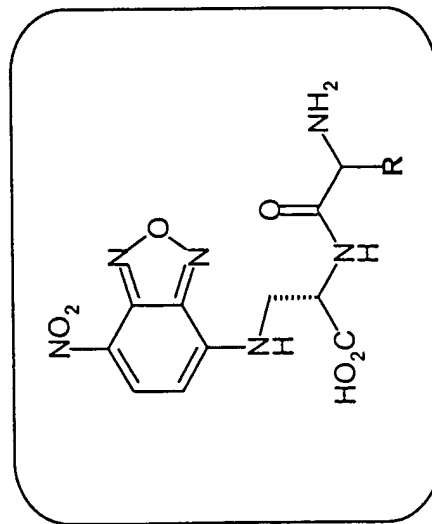
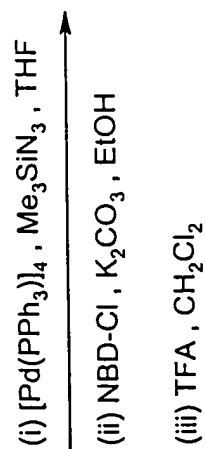
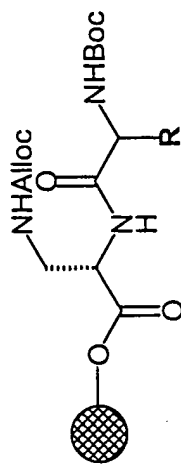


FIG. 14

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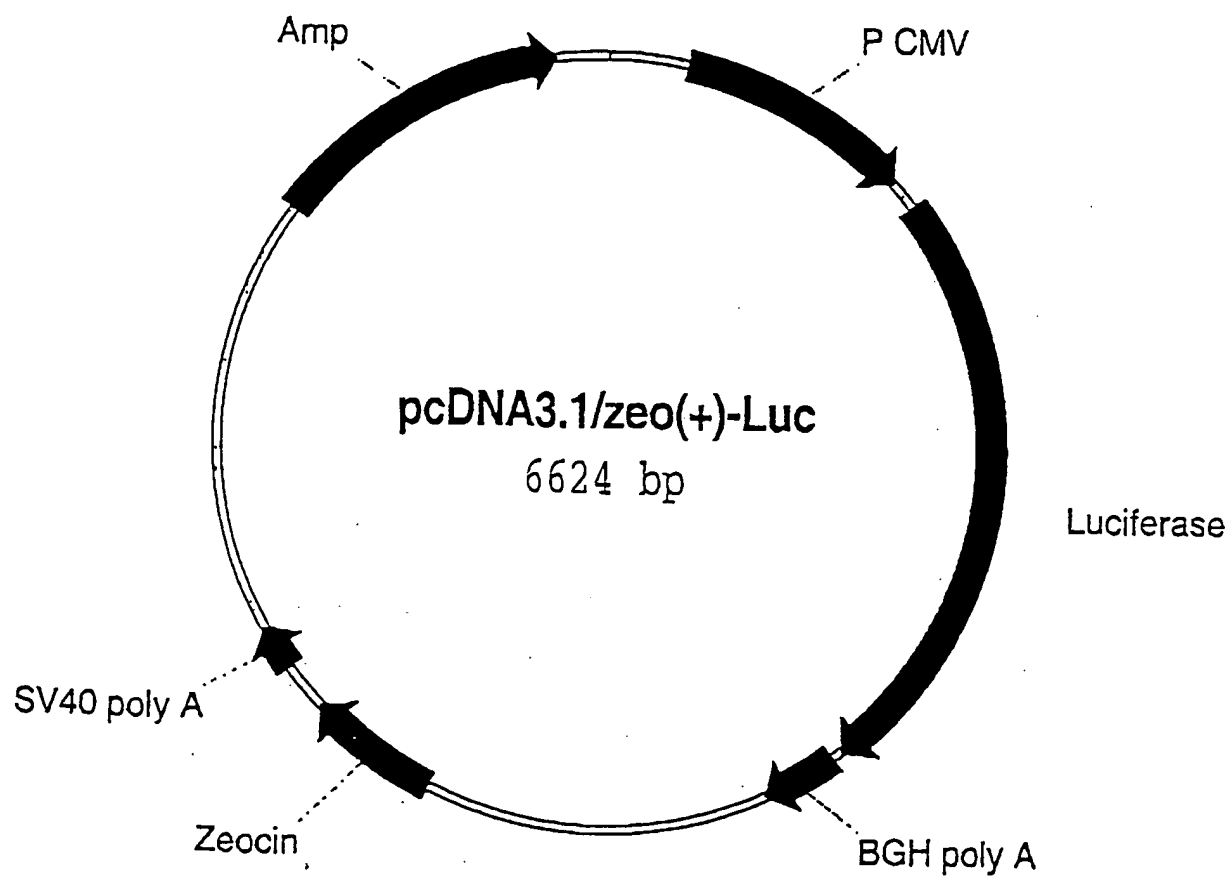


FIG. 15

Synthesis of Luciferin-Conjugated Dipeptide GP5-71

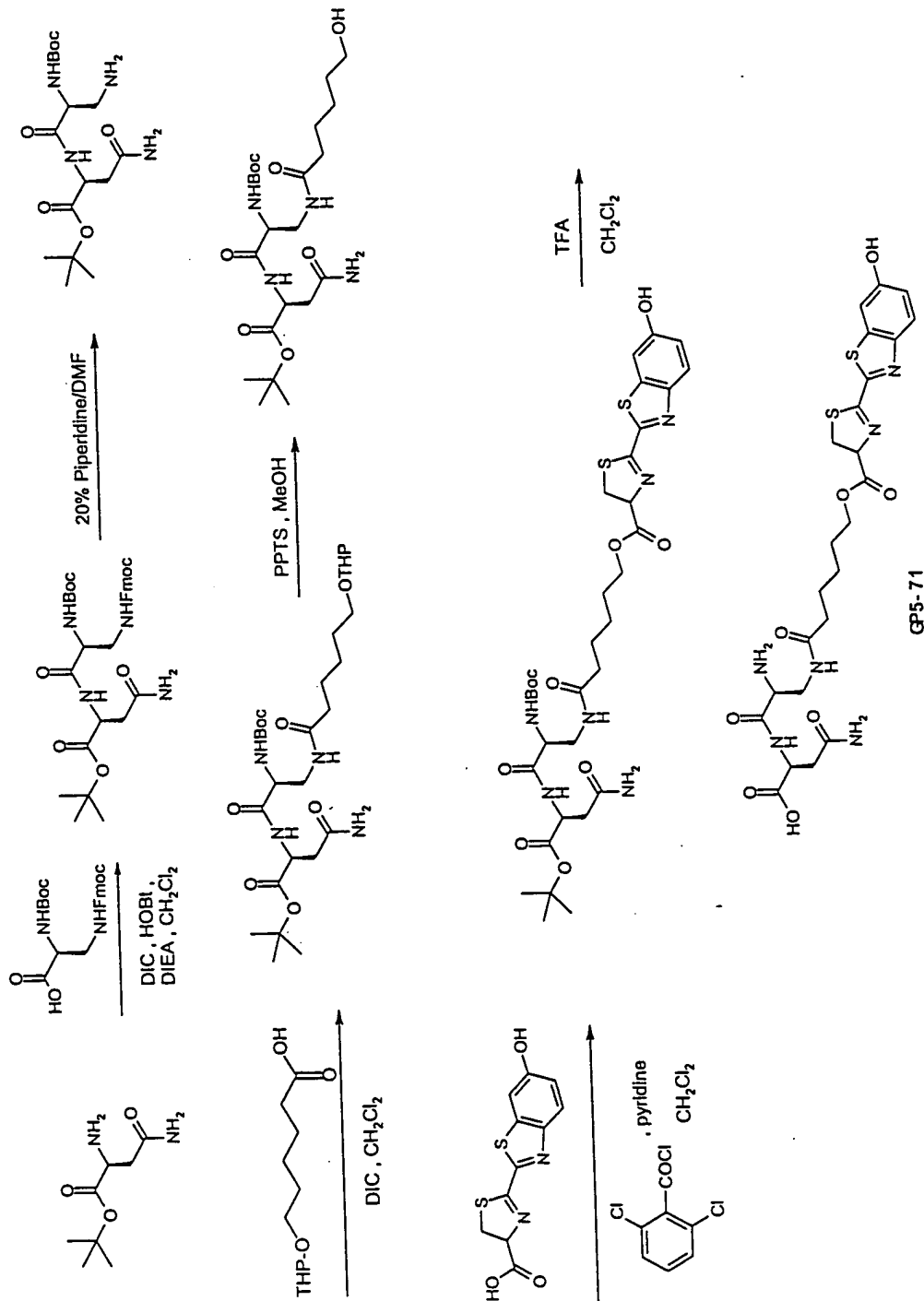


Fig. 16

Synthesis of Luciferin-Glycocholate Ester Conjugate CZ15-73

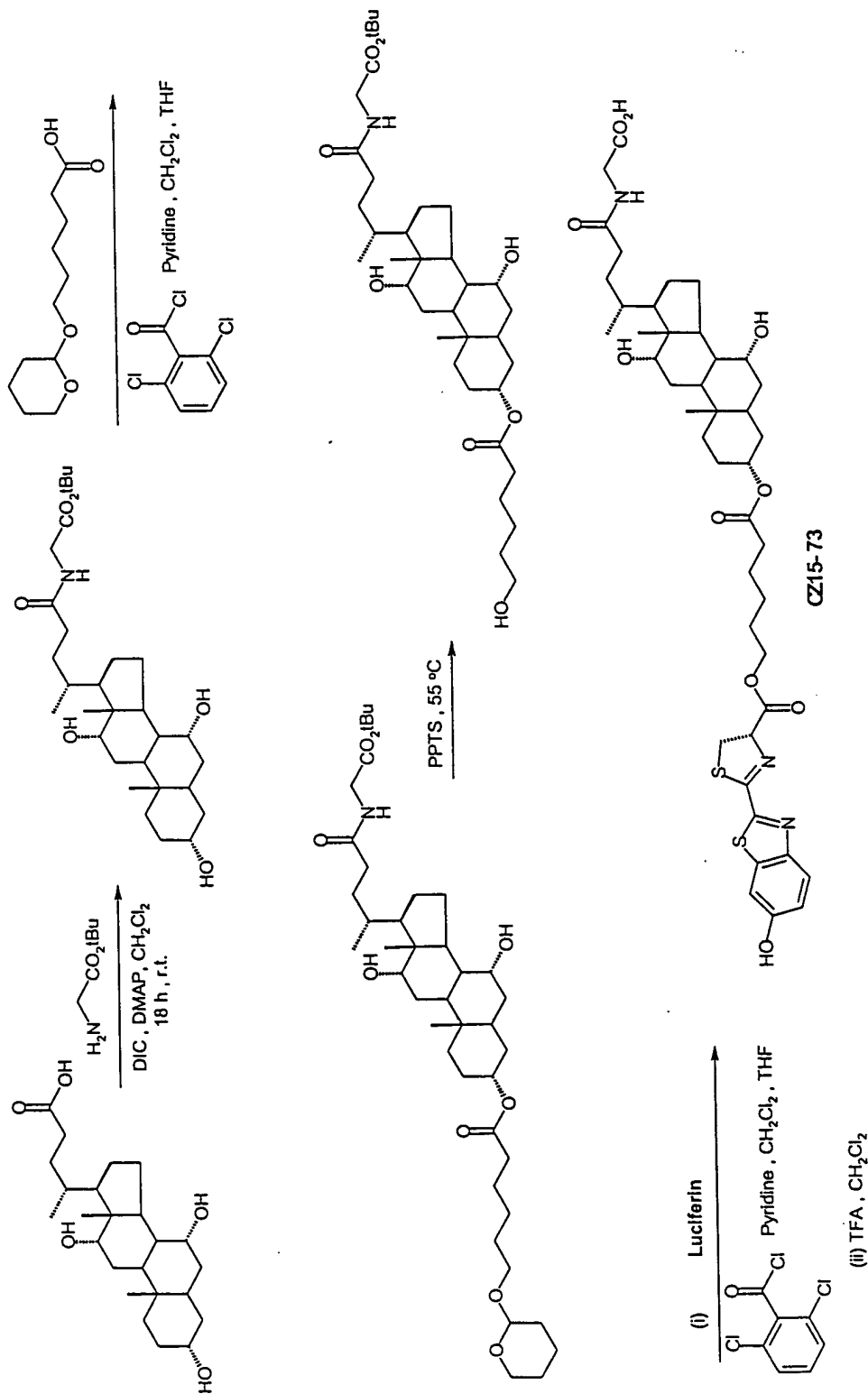
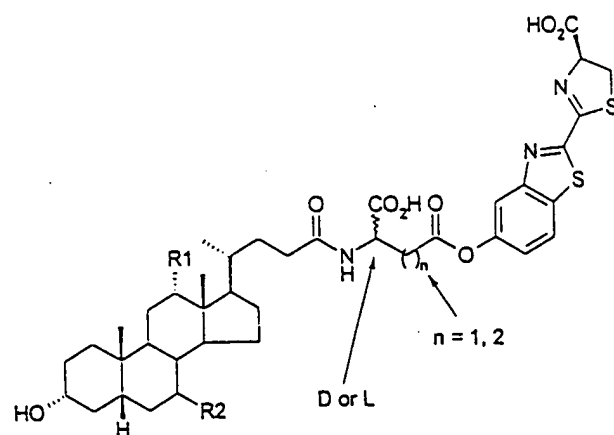


FIG. 17

Bile Acid - Luciferin Conjugate Library



- (i) R1 = OH; R2 = α -OH
- (ii) R1 = OH; R2 = H
- (iii) R1 = H; R2 = α -OH
- (iv) R1 = H; R2 = β -OH
- (v) R1 = H; R2 = H

FIG. 18

Synthesis of Conditionally Fluorescent Dipeptide GP5-77

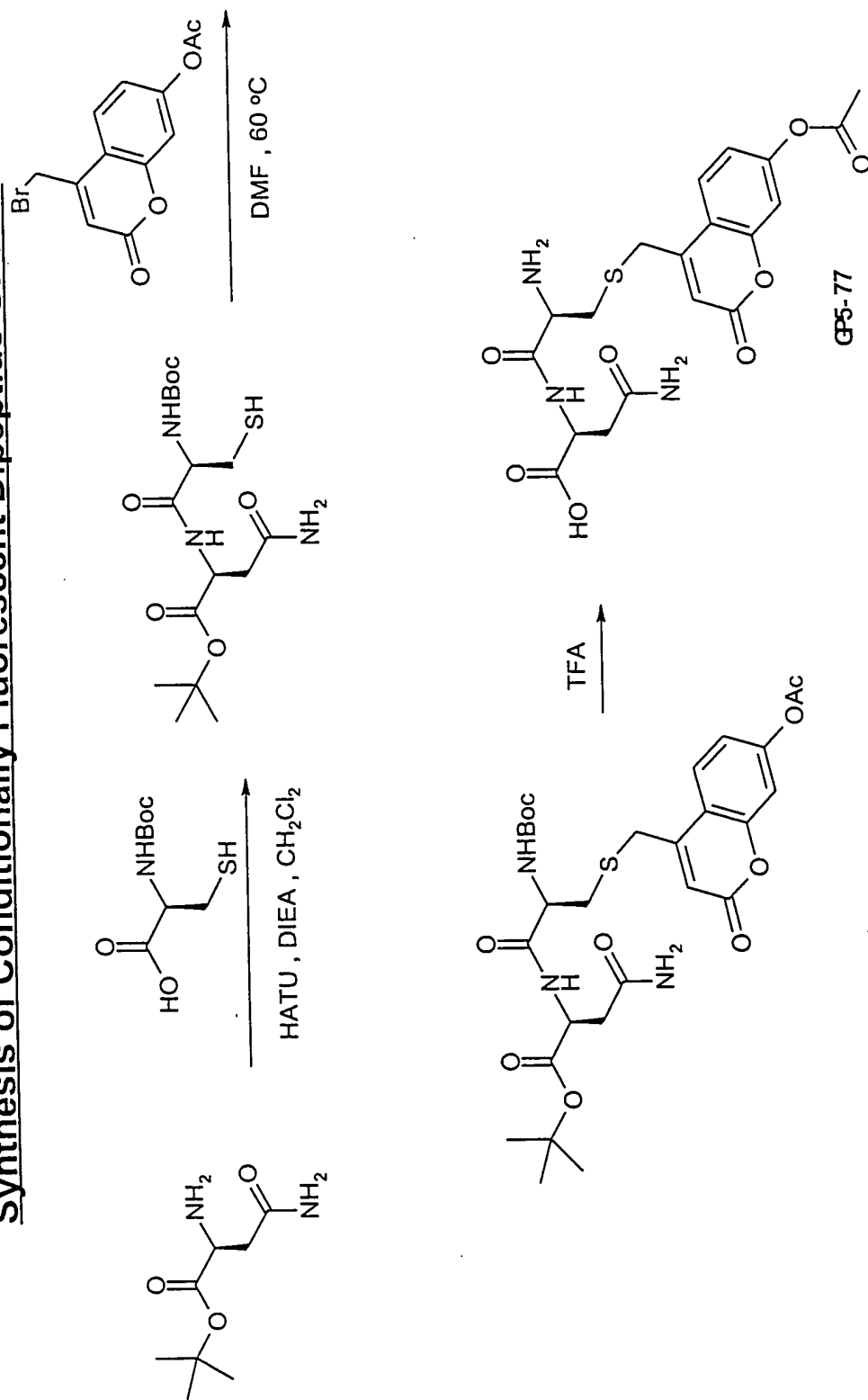


FIG. 2D

Synthesis of Conditionally Fluorescent Dipeptide GP5-00

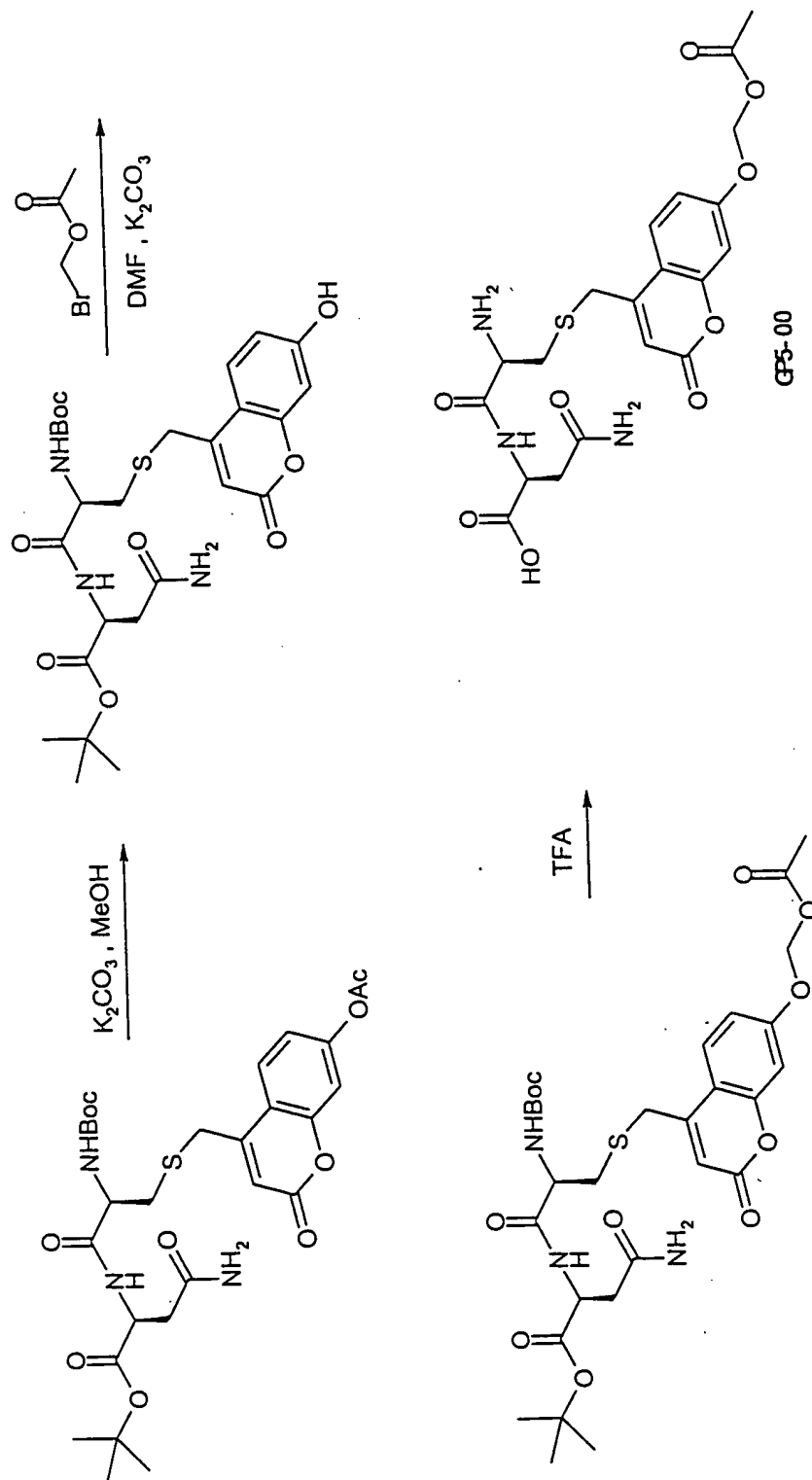


FIG. 21

Preparation of Cholyl-L-Lys-(ϵ -NBD)-OH

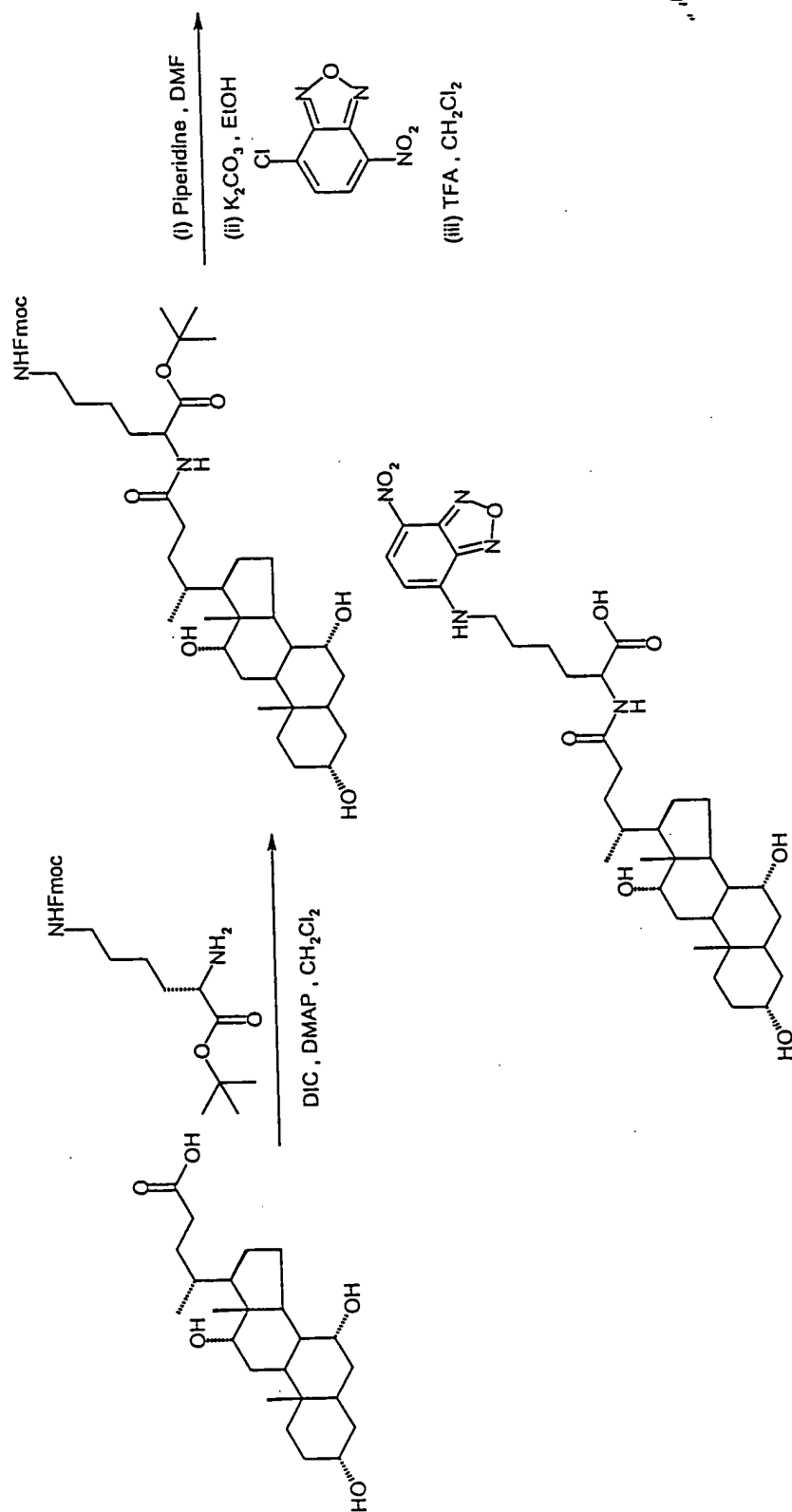


Fig. 22

Preparation of Cholestyl-Lysine Conjugate of Naproxen

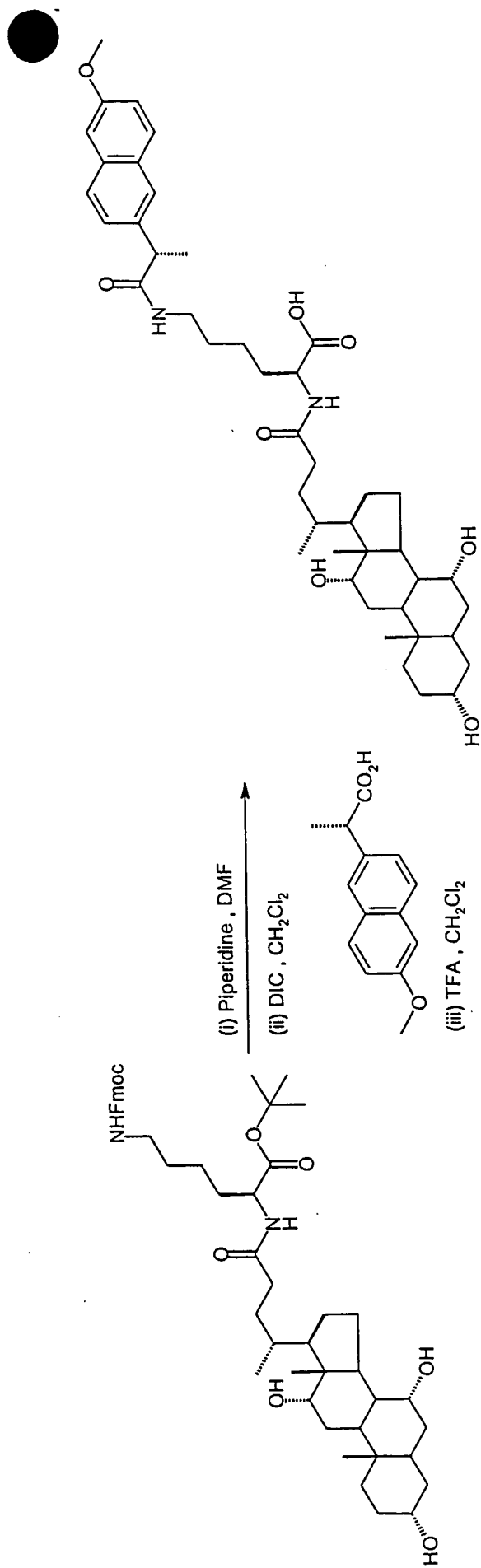


FIG. 23

Preparation of Cholyl L-Dopa

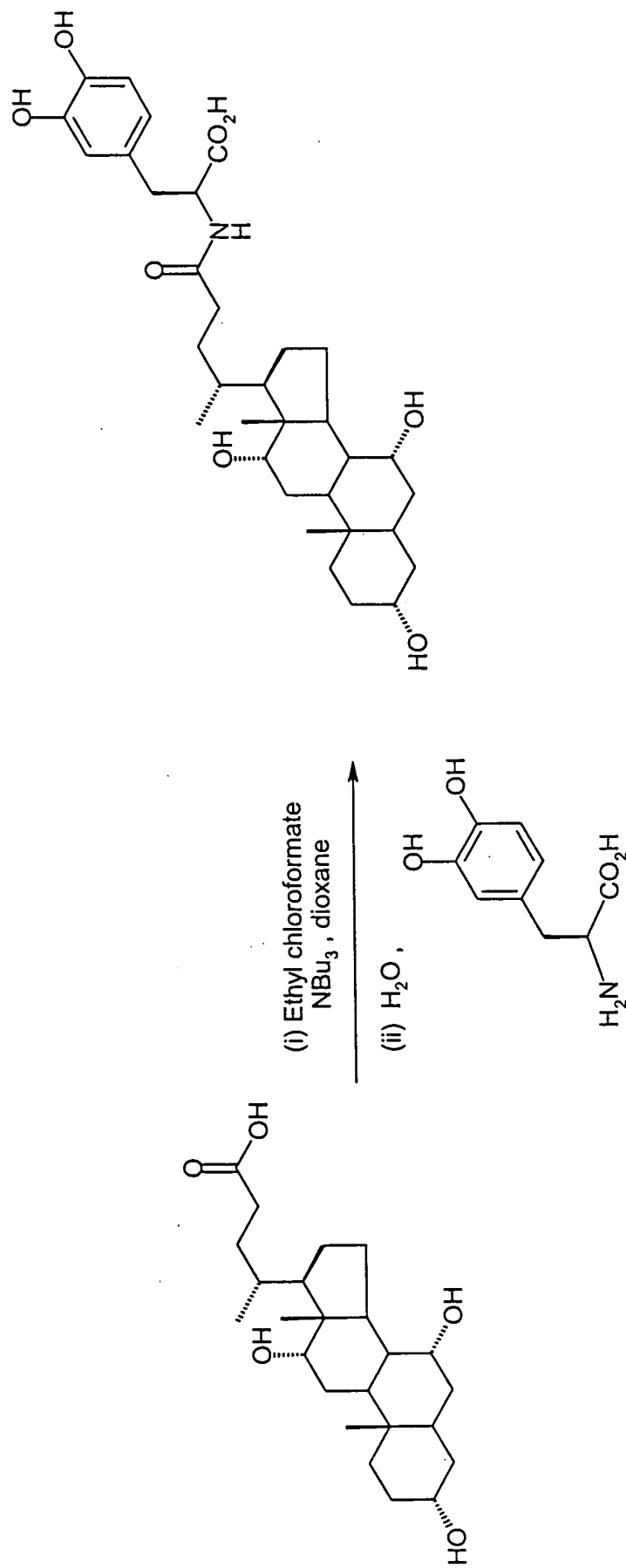


Fig. 24

004750-225T9960

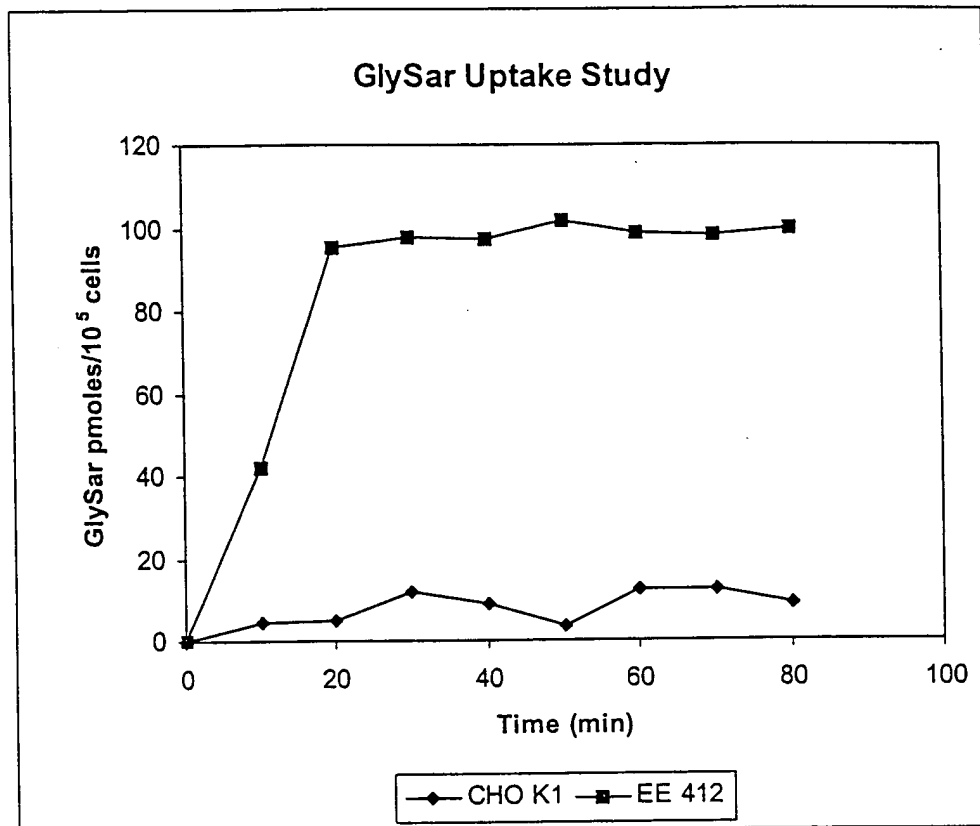


FIG. 25

Trans-stimulation Assays

³H-GlySar efflux by unlabeled GlySar in CHO-PEPT1 cells

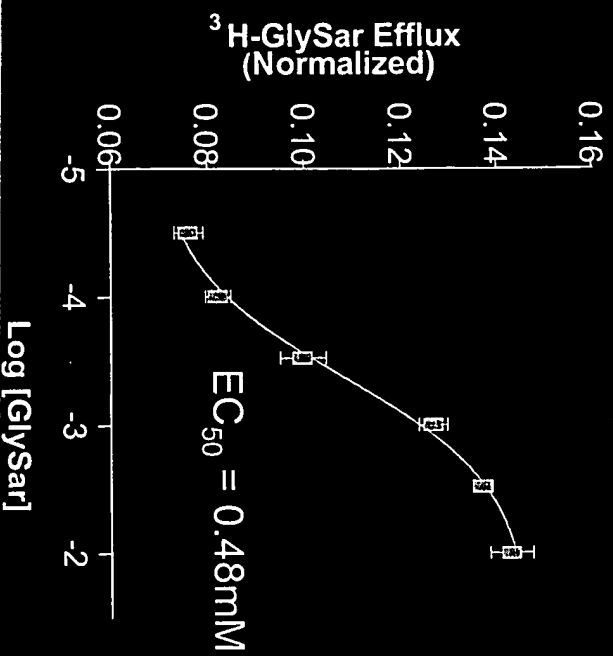


FIG. 26 A

³H-Taurocholate efflux by Cholate analogs in CHO-LBAT cells

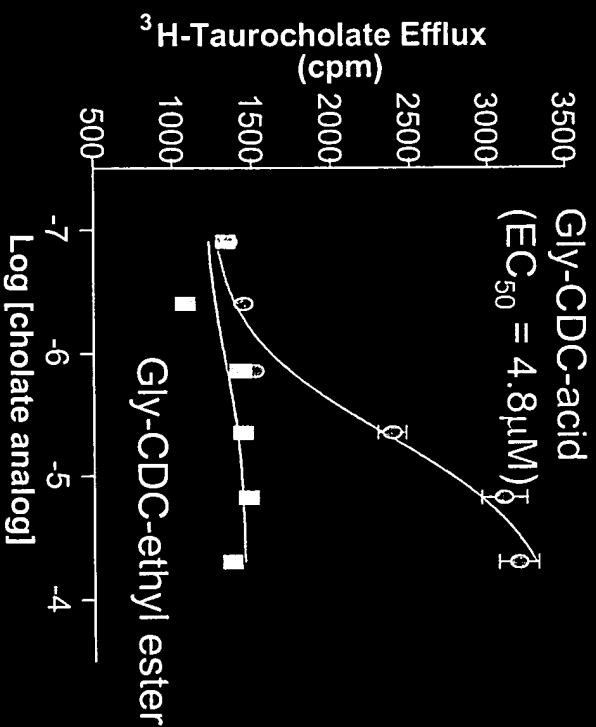
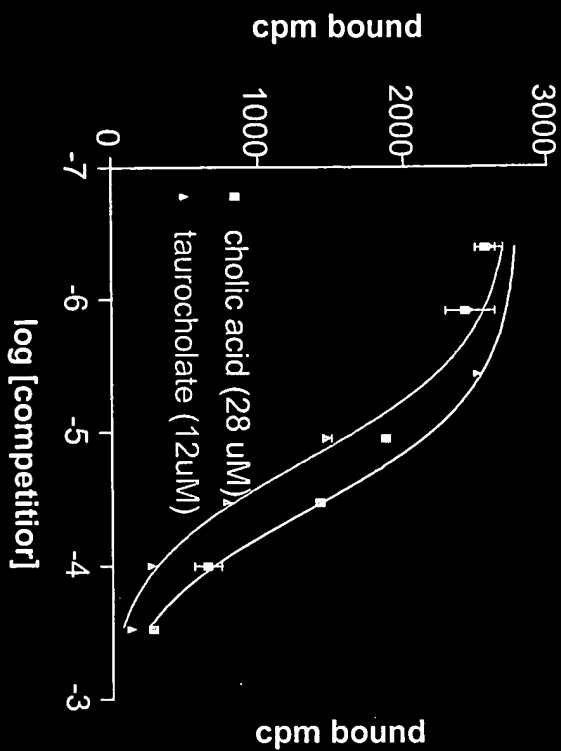


FIG. 26 B

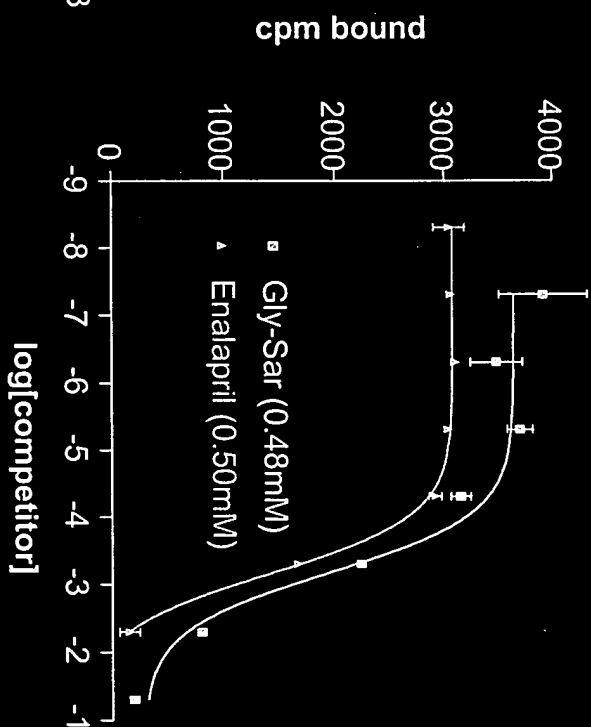
Inhibitory Activity of Known Substrates

³H-Taurocholate Inhibition CHO-IBAT



Fla. 27A

³H-Gly-Sar Inhibition CHO-PEPT1



Fla. 27B

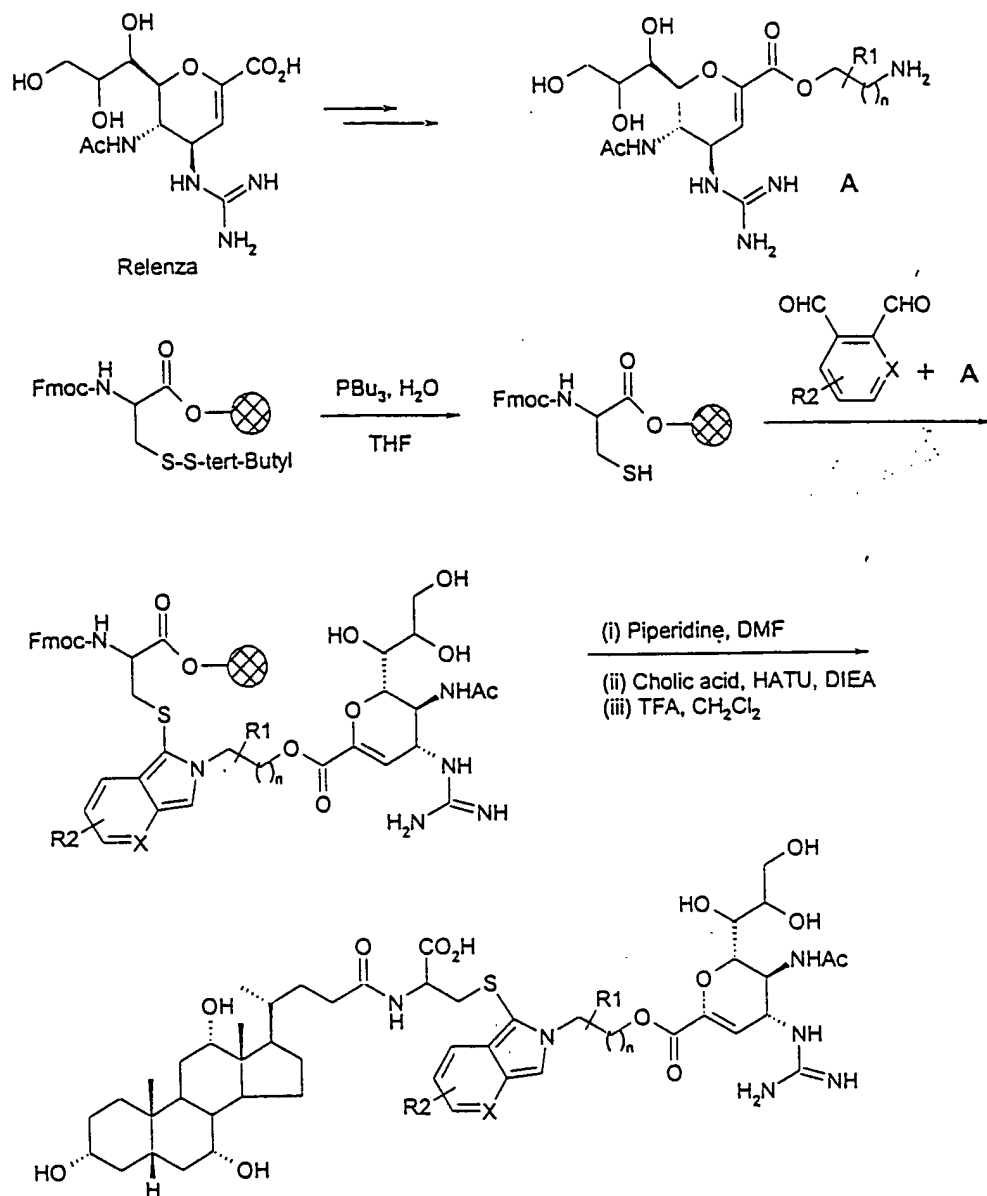


FIG. 28

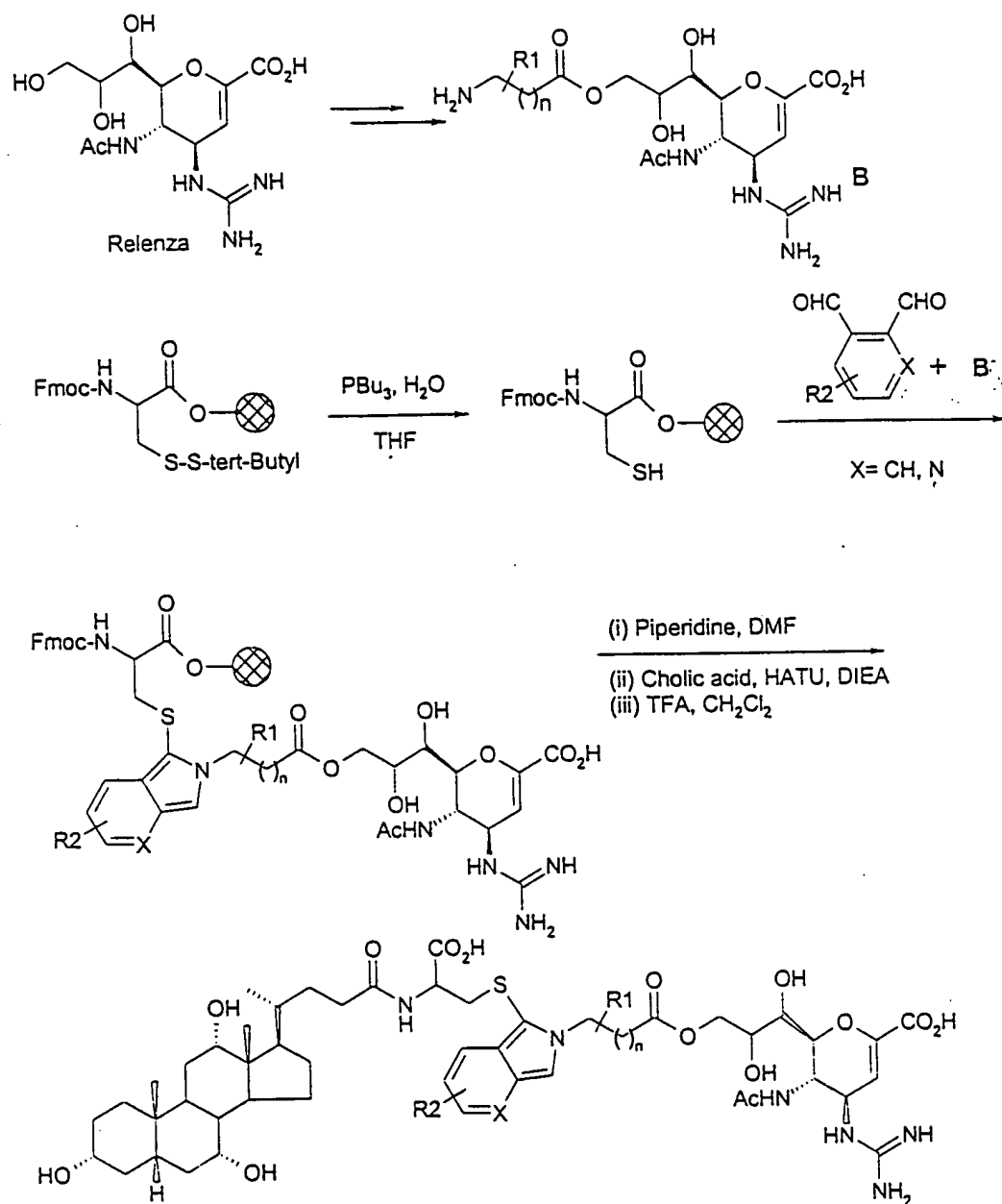


FIG. 29

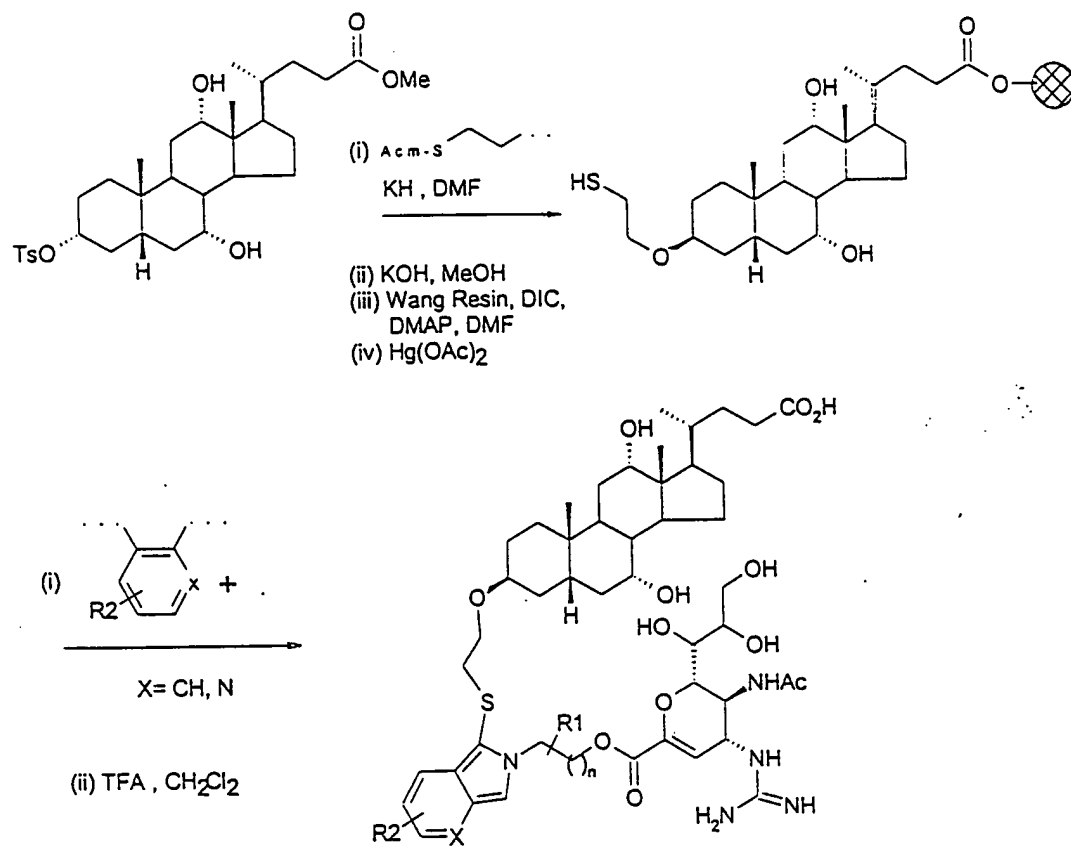


FIG. 30